

## ABSTRACT

5       Methods and compositions for performing RNA interference comprising a wide  
variety of stabilized polynucleotides suitable for use in serum-containing media and for *in*  
*vivo* applications, such as therapeutic applications, are provided. These polynucleotides  
permit effective and efficient applications of RNA interference to applications such as  
diagnostics and therapeutics through the use of one or more modifications including  
orthoesters, terminal conjugates, modified linkages and 2' modified nucleotides.

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